



SARS: Aetiology

JSM Peiris & Y Guan,
The University of Hong Kong

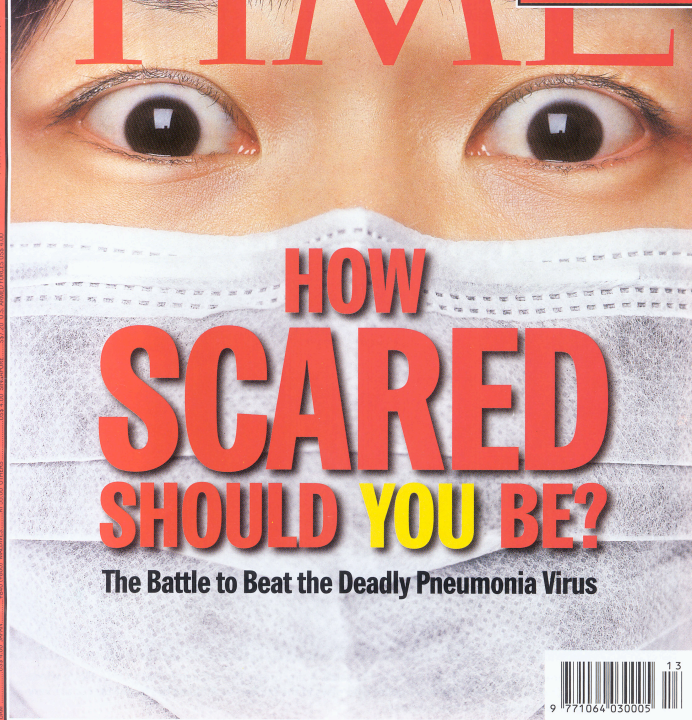
WHO SARS Laboratory Network

APRIL 7, 2003

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INSIDE: 40 PAGES OF WAR COVERAGE

TIME



HOW
SCARED
SHOULD YOU BE?

The Battle to Beat the Deadly Pneumonia Virus



www.timeasia.com



Early February 2003

- Surveillance of severe atypical pneumonia in Hospital Authority in Hong Kong
- Initiate investigation in Guangdong



Late February / Early March

- Late Feb: Outbreak in Hanoi
- Outbreak in Singapore and Canada - Hong Kong returnees
- Early March: Outbreak in health care workers in Hong Kong
- 12 March: WHO Global Alert on SARS
- March 17: WHO Network of SARS Laboratories

Aetiology

- Influenza and other conventional respiratory pathogens ruled-out
- Strategy:
 - unconventional cell lines to grow the virus
 - consensus primer / low stringency PCR
 - random primer RT-PCR / differential display
 - Electron microscopy on lung biopsy
 - *Array technology*

A Novel coronavirus is associated with SARS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome

Christian Drosten, M.D., Stephan Günther, M.D., Wolfgang Preiser, M.D., Sylvie van der Werf, Ph.D., Hans-Reinhard Brodt, M.D., Stephan Becker, Ph.D., Holger Rabenau, Ph.D., Marcus Panning, M.D., Larissa Kolesnikova, Ph.D., Ron A.M. Fouchier, Ph.D., Annemarie Berger, Ph.D., Ana-Maria Burguière, Ph.D., Jindrich Cinatl, Ph.D., Markus Eickmann, Ph.D., Nicolas Escriou, Ph.D., Klaus Grywna, M.Sc., Stefanie Kramme, M.D., Jean-Claude Manuguerra, Ph.D., Stefanie Müller, M.Sc., Volker Rickerts, M.D., Martin Stürmer, Ph.D., Simon Vieth, Hans-Dieter Klenk, M.D., Albert D.M.E. Osterhaus, Ph.D., Herbert Schmitz, M.D., and Hans Wilhelm Doerr, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome

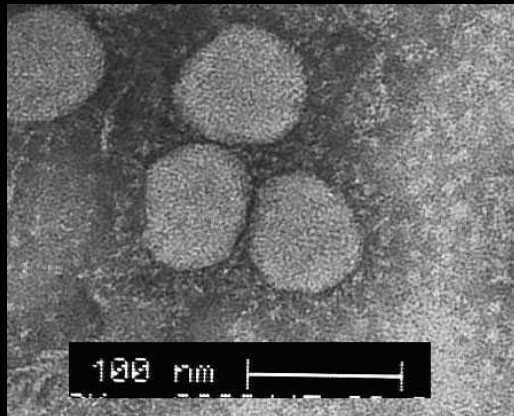
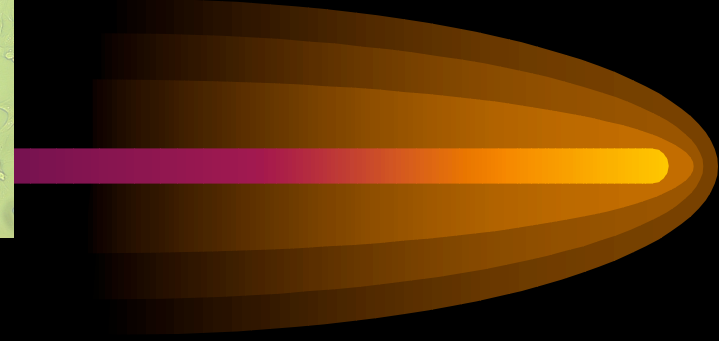
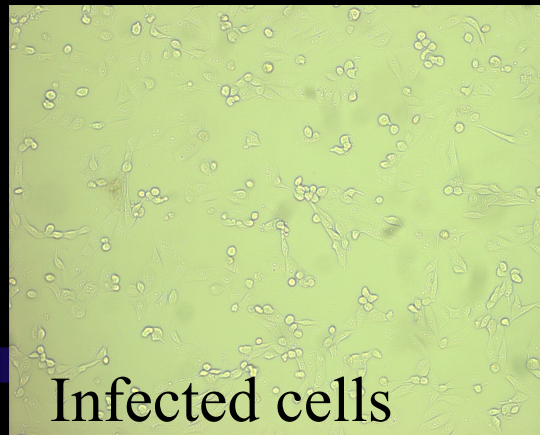
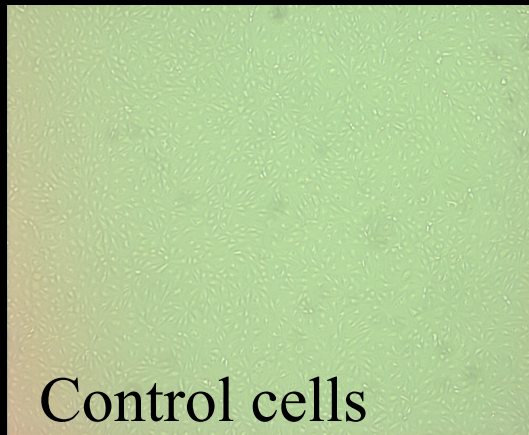
Thomas G. Ksiazek, D.V.M., Ph.D., Dean Erdman, Dr. P.H., Cynthia Goldsmith, M.S., Sherif R. Zaki, M.D., Ph.D., Teresa Peret, Ph.D., Shannon Emery, Suxiang Tong, Ph.D., Carlo Urbani, M.D.,* James A. Comer, Ph.D., M.P.H., Wilina Lim, Pierre E. Rollin, M.D., Scott Dowell, M.D., M.P.H., Ai-Ee Ling, M.D., Charles Humphrey, Ph.D., Wun-Ju Shieh, M.D., Jeannette Guarner, M.D., Christopher D. Paddock, M.D., Paul Rota, Ph.D., Barry Fields, Ph.D., Joseph DeRisi, Ph.D., Jyh-Yuan Yang, Ph.D., Nancy Cox, Ph.D., James Hughes, M.D., James W. LeDuc, Ph.D., William Bellini, Ph.D., Larry J. Anderson, M.D., and the SARS Working Group†

ARTICLES

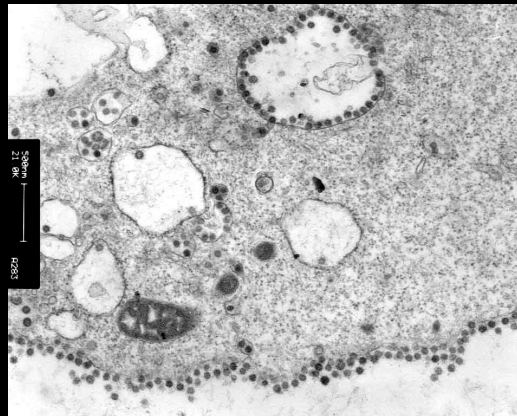
Articles

🌐👤 Coronavirus as a possible cause of severe acute respiratory syndrome

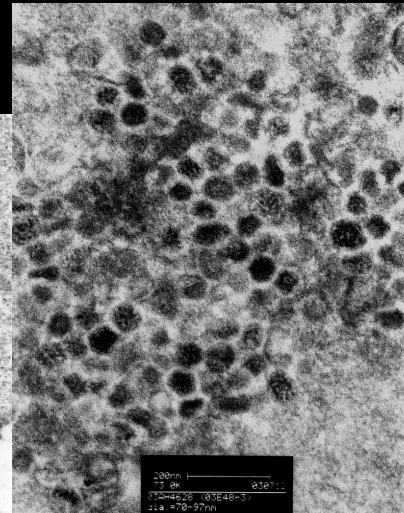
J S M Peiris, S T Lai, L L M Poon, Y Guan, L Y C Yam, W Lim, J Nicholls, W K S Yee, W W Yan, M T Cheung, V C C Cheng, K H Chan, D N C Tsang, R W H Yung, T K Ng, K Y Yuen, and members of the SARS study group*



Negative stain
Cultured virus



Thin sect
Cultured virus



Direct EM
Lung Bx virus

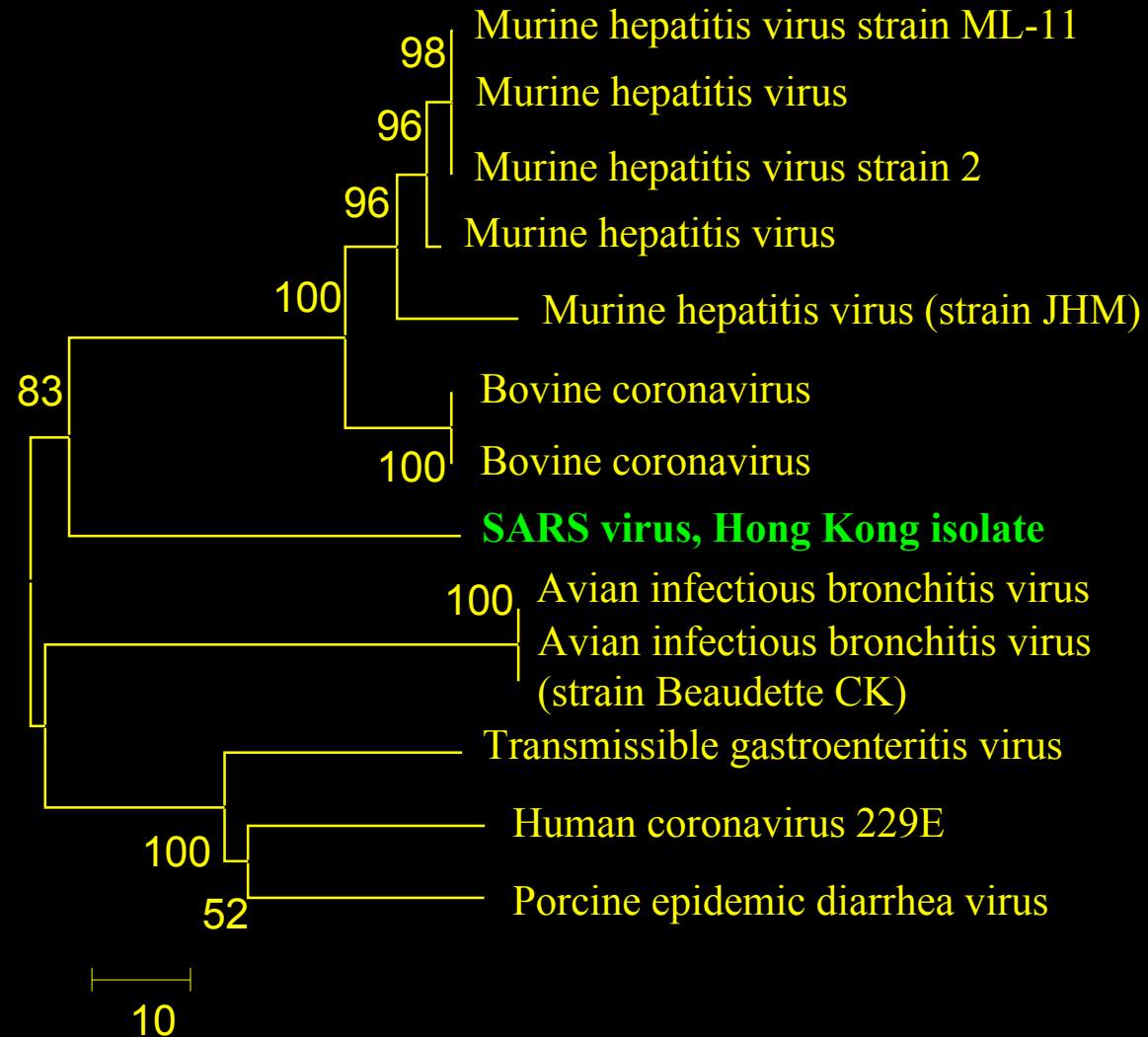
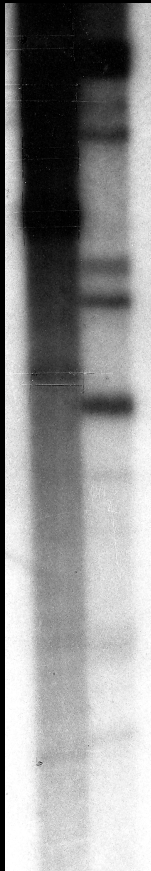


Thin sect
Cultured virus

Coronavirus-like agent is isolated

Detection of SARS sequence by random RT-PCR

- A 646 nt sequence of coronavirus origin



Genome of the SARS-associated coronavirus

Scienceexpress

Research Article

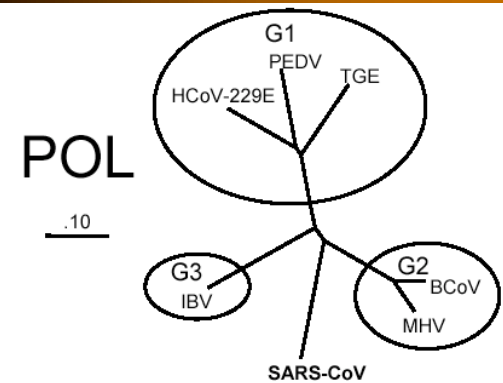
The Genome Sequence of the SARS-Associated Coronavirus

Marco A. Marra,^{1*} Steven J. M. Jones,¹ Caroline R. Astell,¹ Robert A. Holt,¹ Angela Brooks-Wilson,¹ Yaron S. N. Butterfield,¹ Jaswinder Khattri,¹ Jennifer K. Asano,¹ Sarah A. Barber,¹ Susanna Y. Chan,¹ Alison Cloutier,¹ Shaun M. Coughlin,¹ Doug Freeman,¹ Noreen Girn,¹ Obi L. Griffith,¹ Stephen R. Leach,¹ Michael Mayo,¹ Helen McDonald,¹ Stephen B. Montgomery,¹ Pawan K. Pandoh,¹ Anca S. Petrescu,¹ A. Gordon Robertson,¹ Jacqueline E. Schein,¹ Asim Siddiqui,¹ Duane E. Smailus,¹ Jeff M. Stott,¹ George S. Yang¹

Francis Plummer,² Anton Andonov,² Harvey Artsob,² Nathalie Bastien,² Kathy Bernard,² Timothy F. Booth,² Donnie Bowness,² Michael Drebot,² Lisa Fernando,² Ramon Flick,² Michael Garbutt,² Michael Gray,² Allen Grolla,² Steven Jones,² Heinz Feldmann,² Adrienne Meyers,² Amin Kabani,² Yan Li,² Susan Normand,² Ute Stroher,² Graham A. Tipples,² Shaun Tyler,² Robert Vogrig,² Diane Ward,² Brynn Watson²

Robert C. Brunham,³ Mel Krajden,³ Martin Petric,³ Danuta M. Skowronski³

Chris Upton,⁴ Rachel L. Roper⁴

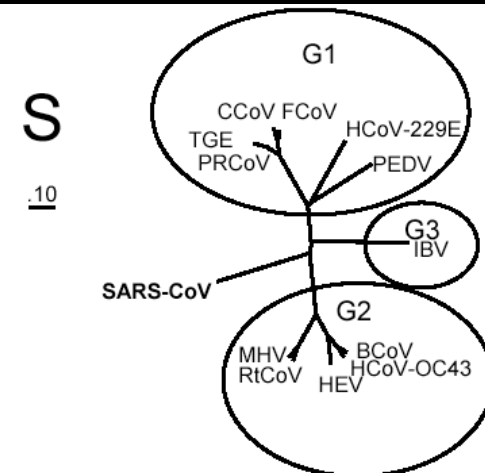


Scienceexpress

Research Article

Characterization of a Novel Coronavirus Associated with Severe Acute Respiratory Syndrome

Paul A. Rota,^{1*} M. Steven Oberste,¹ Stephan S. Monroe,¹ W. Allan Nix,¹ Ray Campagnoli,¹ Joseph P. Icenogle,¹ Silvia Peñaranda,¹ Bettina Bankamp,¹ Kaija Maher,¹ Min-hsin Chen,¹ Suxiong Tong,¹ Azaibi Tamin,¹ Luis Lowe,¹ Michael Frace,¹ Joseph L. DeRisi,² Qi Chen,¹ David Wang,² Dean D. Erdman,¹ Teresa C. T. Peret,¹ Cara Burns,¹ Thomas G. Ksiazek,¹ Pierre E. Rollin,¹ Anthony Sanchez,¹ Stephanie Liffick,¹ Brian Holloway,¹ Josef Limor,¹ Karen McCaustland,¹ Melissa Olsen-Rasmussen,¹ Ron Fouchier,³ Stephan Günther,⁴ Albert D. M. E. Osterhaus,³ Christian Drosten,⁴ Mark A. Pallansch,¹ Larry J. Anderson,¹ William J. Bellini¹



*Koch's postulates:
Association of microbe and disease*

SEROLOGY:

- 107 patients with clinically defined SARS
 - Rising titre to coronavirus 104 / 107 (97%)
 - Rising IFA titre to human metapneumovirus
0 / 50 (0%)
- 45 paired sera from non-SARS patients: no antibody to CV
- 200 blood donors: no antibody

SARS-coronavirus in macaques

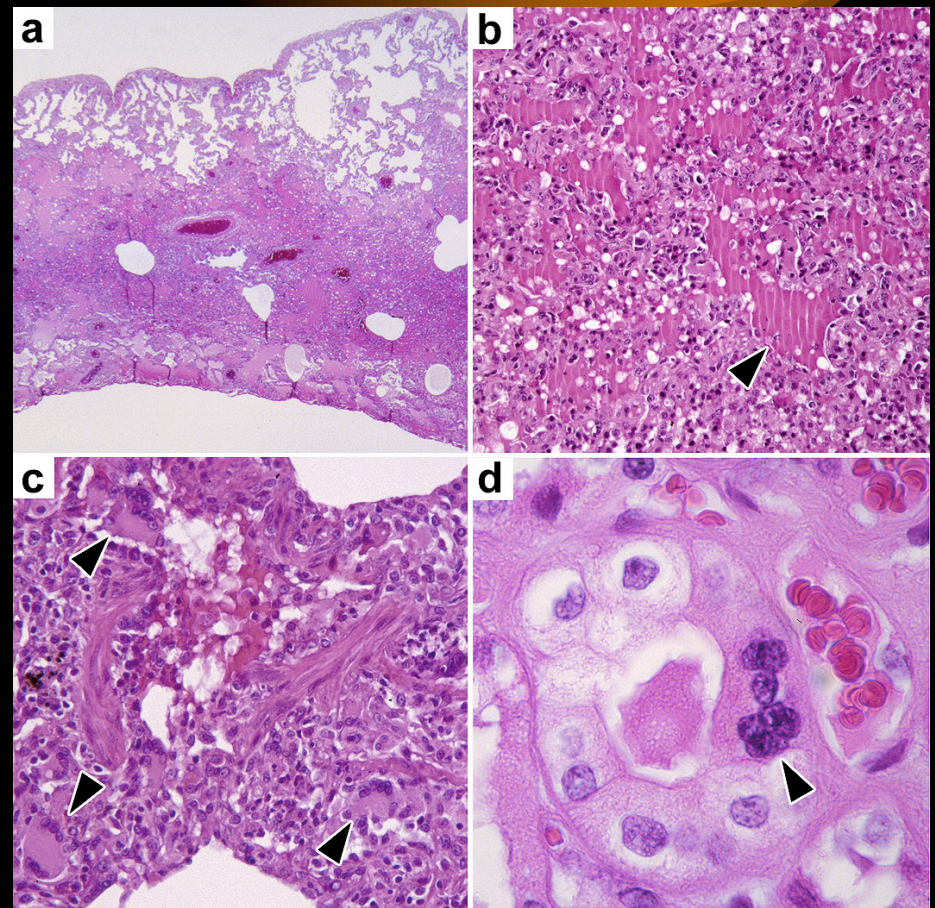
Macaque # 4:

Severe multifocal pulmonary consolidation

Coronavirus detected in lung tissue

Severe interstitial pneumonia

Fouchier et al - Nature 2003, on line



Questions



- Sites and duration of virus shedding and infectivity
- Stability of virus in environment
- Molecular evolution: how many lineages contribute to the Hong Kong outbreak ?
- Animal reservoir

Viral load in SARS patients

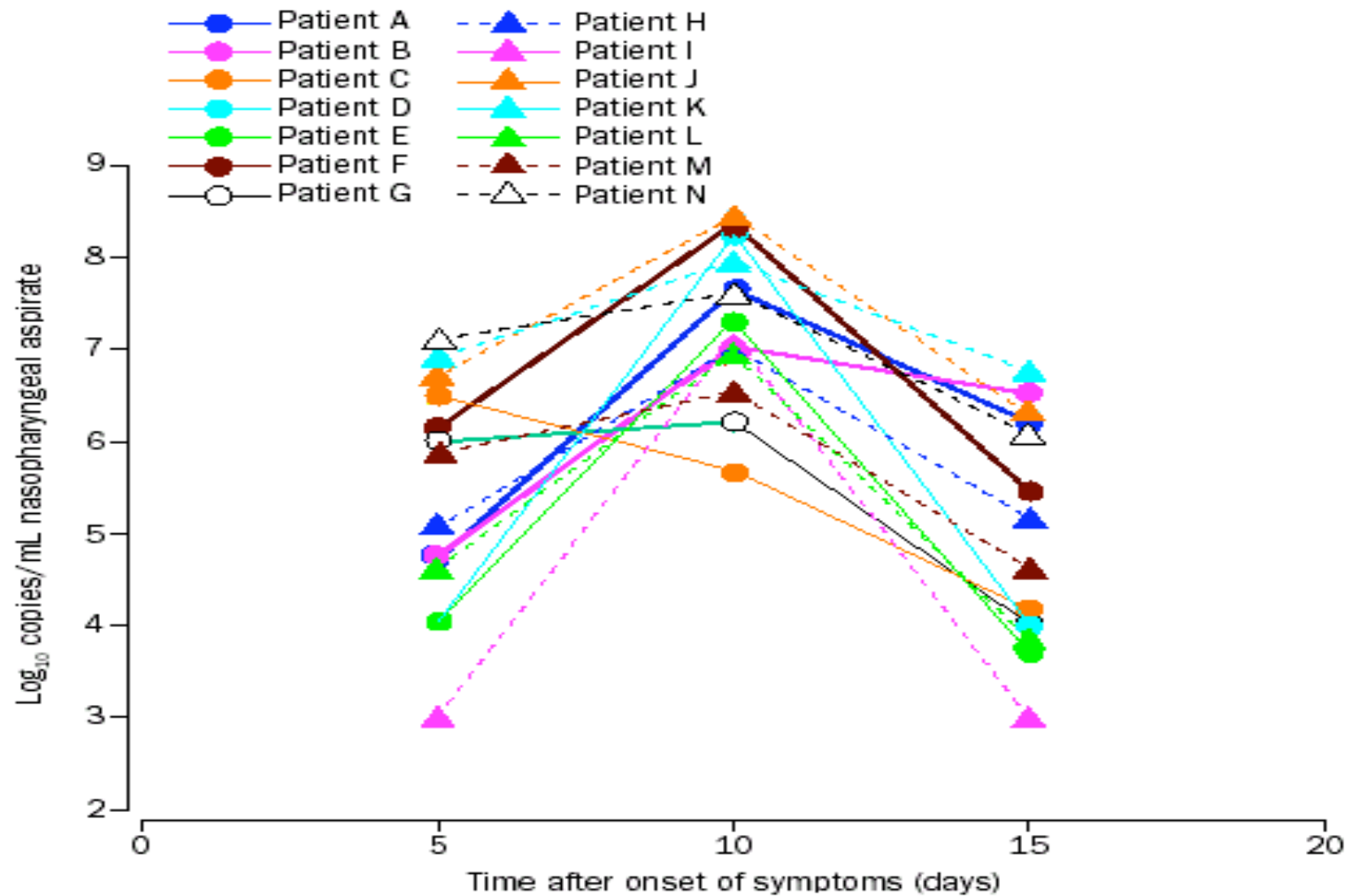


Figure 4: **Sequential quantitative RT-PCR for SARS-associated coronavirus in nasopharyngeal aspirates of 14 SARS patients**

Implications

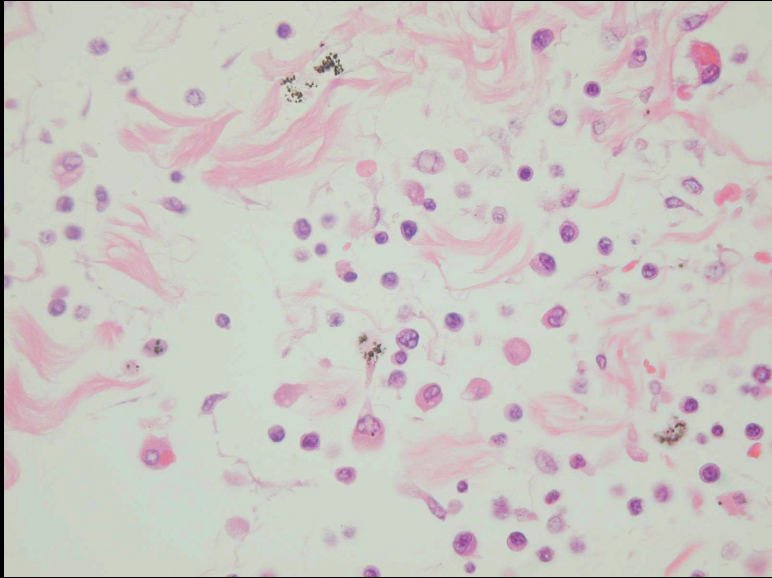
- **Lab Diagnosis: Virus detection (RT-PCR or other):**
 - **Viral load is lower in first 5 days of illness. A challenge for diagnosis.**
- **Transmission: more likely in later phase of illness?**

Virus stability: Implications for transmission and infection control

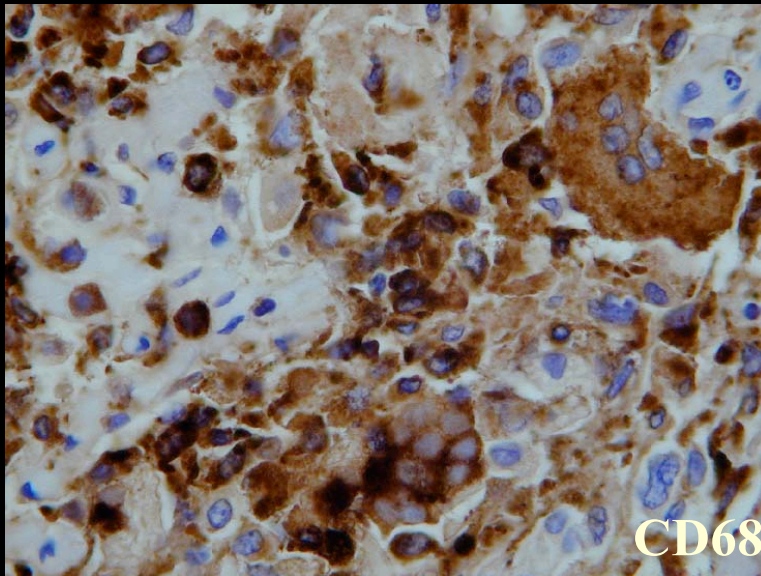
- The virus is more stable in environment than other respiratory viruses
- Infectious virus can survive
 - dried: 1-2 days on surfaces at room temperature
 - non-porous > porous
 - organic matter (eg faeces) increases stability
- Animal coronaviruses are infectious for long periods in environment

Fomites: a route of transmission?

Lung Pathology



Haemophagocytosis



Giant cells of
macrophage origin

Nicholls et al (2003) Lancet

CD68

Questions

- Sites and duration of virus shedding and infectivity
- Stability of virus in environment
- Molecular evolution: how many lineages contribute to the Hong Kong outbreak ?
- **Animal reservoir**
 - Isolation of SARS-CoV-like virus from civets cats and a racoon-dog:
 - Y Guan: Epidemiology session

WHO Network of Laboratories

- **Federal Laboratories for Health Canada, Winnipeg, Canada**
- **Health Canada, Ottawa, Canada**
- **Public Health Laboratory Centre, Hongkong SAR China**
- **Prince of Wales Hospital, Hongkong SAR China**
- **The University of Hongkong, Hong Kong SAR, China**
- **Institut Pasteur, Paris, France**
- **Bernhard-Nocht Institute, Hamburg and Johann Wolfgang Goethe Universitat, Frankfurt, Germany**
- **National Institute of Infectious Disease, Tokyo, Japan**
- **Erasmus MC, Rotterdam, The Netherlands**
- **Singapore General Hospital, Singapore**
- **Central Public Health Laboratory, London, UK**
- **Centers for Disease Control & Prevention, Atlanta, USA**

Acknowledgements



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